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- (71) Applicant (for all designated States except US): CAR-DIOME INC. [US/US]; Suite 1113, 1111 Brickell Avenue, Miami, FL 33131 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): FEDIDA, David [CA/CA]; 3375 West 2nd Avenue, Vancouver, British Columbia V6R 1H9 (CA). STEELE, David [CA/CA]; 1958 West 42nd Avenue, Vancouver, British Columbia V6M 2B1 (CA).
- (74) Agents: LITTLEFIELD, Otis, B. et al.; Morrison & Forster LLP, 425 Market Street, San Francisco, CA 94105-2482 (US).
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(54) Title: MUTATIONS OF VOLTAGE-GATED ION CHANNELS THAT ALLOW THEM TO EXPRESS A VOLTAGE-INDEPENDENT PHENOTYPE AND AN IMPROVED METHOD TO USE THE SAME

Alignment of Voltage-Gated Potassium Channels Relevant Regions

hKv1.1	PYFITLGTFLAEQ-----FGNQKGEQATSLATLRYTRIVRVTRFKLSRHSGK
mKv1.2	PYFITLGTFLAEKP-----EDAQQQQAMSLALRYIRLVRFRIKLSRHSGK
Kv1.4	PYFITLGTFLAEQGG-----GNGQQQAMSPATLRIIRLVRFRIKLSRHSGK
Kv1.3	PYFITLGTFLAEQ-----GNGQQAMSLALRYIRLVRFRIKLSRHSGK
hKv1.5	PYFITLGTFLAEQGG-----GNGQQQAMSLALRYIRLVRFRIKLSRHSGK
ShakerB	PYFITLGTFLAEQGG-----GNGQQQAMSLALRYIRLVRFRIKLSRHSGK
rKv3.1	PYFLEVC-----LSCLSKAAKDVLCFLRVRFRIKLSRHSGK
rKv2.1	PYFVTFLESHKS-----VLQFQNVRFVTRIRIRILKLSRHSGK
hKv4.2	PYYIGLVMTENEDVS-----GAFVIRLVRFRIKLSRHSGK
hKv1.1	LQILGQTLKASHRELGLLIFFLFGVTLFSSAVYFAEAD-----FASHFSSIFDA
mKv1.2	LQILGQTLKASHRELGLLIFFLFGVTLFSSAVYFAEAD-----ERSCFSSIFDA
Kv1.4	LQILGQTLKASHRELGLLIFFLFGVTLFSSAVYFAEAD-----ECTHFSIFDA
Kv1.3	LQILGQTLKASHRELGLLIFFLFGVTLFSSAVYFAEAD-----DPTSGFSSIFDA
hKv1.5	LQILGQTLKASHRELGLLIFFLFGVTLFSSAVYFAEAD-----NOOTHFSSIFDA
ShakerB	LQILGQTLKASHRELGLLIFFLFGVTLFSSAVYFAEAD-----SEAFSSIFDA
rKv3.1	LRVLGHTLRASHRELGLLIFFLFGVTLFSSAVYFAEAD-----EDDTERKSFDA
rKv2.1	LQSLGPTLRASHRELGLLIFFLFGVTLFSSAVYFAEAD-----SSASKPTSIFDA
hKv4.2	LRILGVTLSKASHRELGLLIFFLFGVTLFSSAVYFAEAD-----SSASKPTSIFDA
hKv1.1	PWAVVSMITVGYGDMPTTIGGKIVGSLCAIAGVLTIALPFWIVSNFHYFHRTEGE
mKv1.2	PWAVVSMITVGYGDMPTTIGGKIVGSLCAIAGVLTIALPFWIVSNFHYFHRTEGE
Kv1.4	PWAVVSMITVGYGDMPTTIGGKIVGSLCAIAGVLTIALPFWIVSNFHYFHRTEGE
Kv1.3	PWAVVSMITVGYGDMPTTIGGKIVGSLCAIAGVLTIALPFWIVSNFHYFHRTEGE
hKv1.5	PWAVVSMITVGYGDMPTTIGGKIVGSLCAIAGVLTIALPFWIVSNFHYFHRTEGE
ShakerB	PWAVVSMITVGYGDMPTTIGGKIVGSLCAIAGVLTIALPFWIVSNFHYFHRTEGE
rKv3.1	PWAVVSMITVGYGDMPTTIGGKIVGSLCAIAGVLTIALPFWIVSNFHYFHRTEGE
rKv2.1	PWAVVSMITVGYGDMPTTIGGKIVGSLCAIAGVLTIALPFWIVSNFHYFHRTEGE
hKv4.2	PWAVVSMITVGYGDMPTTIGGKIVGSLCAIAGVLTIALPFWIVSNFHYFHRTEGE

(57) Abstract: The subject invention includes mutant voltage-gated ion channels that are open over a wide range of potential differences across membranes. The present invention also includes methods of use of such mutant voltage-gated ion channels in cells with highly negative potential differences across their membranes. One preferred mutant voltage-gated ion channel is a channel with a mutation at the residue homologous to P513 in Kv1.5 and at least one mutation at one of the residues homologous to R400, R403, and R409 in Kv1.5.

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